

sequence; and a chemical moiety covalently bound to the compound at the at least one non-essential amino acid or mimetic in the consensus sequence and/or the amino acid or mimetic not subject to phosphorylation substituting the canonical Ser or Thr target residue. In these combinatorial libraries, each compound comprises a different chemical moiety.

5 In further embodiments, the present invention is directed to methods of identifying an inhibitor of a protein kinase. The methods comprise creating a combinatorial library as described above for the protein kinase, screening the compounds in the combinatorial library for inhibitory activity of the protein kinase, and identifying any compounds in the combinatorial library that are inhibitors of the protein kinase.

10 The invention is additionally directed to methods of treating a deleterious condition in a mammal that is dependent on a protein kinase for induction or severity. The methods comprise contacting the mammal with an inhibitor of the protein kinase found by any of the above-described methods of identifying an inhibitor of a protein kinase.

The invention is further directed to methods of inhibiting a protein kinase. The methods  
15 comprise contacting the protein kinase with an inhibitor of the protein kinase identified by any of the above-described methods of identifying an inhibitor of a protein kinase.

In other embodiments, the invention is directed to the use of an inhibitor of a protein kinase in the manufacture of a medicament for the treatment of a deleterious condition in a mammal that is dependent on a protein kinase for induction or severity. The treatment comprises  
20 contacting the mammal with an inhibitor of the protein kinase found any of the above-described methods of identifying an inhibitor of a protein kinase.

#### BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows libraries **I – IV** used to identify inhibitors of protein kinase C $\alpha$  (PKC $\alpha$ ).

25 FIG. 2 shows various compounds used in PKC $\alpha$  inhibitor studies.

FIG. 3 is a graph of the inhibition pattern of compound **3** versus variable [ATP].

FIG. 4A-4Z and FIG. 4AA-4JJ shows 720 carboxylic acid moieties used in exemplified invention combinatorial libraries.

FIG. 5 shows 54 aldehyde moieties used in exemplified invention combinatorial libraries.

30 FIG. 6 shows a general scheme for the introduction of molecular diversity at specific amino acid residues on the consensus sequence. The Dap residue [(L)-2,3-diaminopropionic acid] side chain serves as a handle for the assembly of molecular diversity.

FIG. 7 shows control (compound **A**) and lead peptides (**B - G**) derived from libraries **I - IV**. Compound **H** was previously described (1).

35 FIG. 8 shows a reductive alkylation protocol that furnishes molecular diversity at the N-terminus of peptide **6** while retaining a net positive charge at physiological pH. The latter is an